# What Does a "Societal Perspective" Include in Practice? A Systematic Analysis of ICER Assessments in Ultra-Rare Diseases

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# Background

ICER's Ultra-Rare Disease Value Assessment Framework reflects the growing recognition that the full burden of rare disease extends beyond direct healthcare costs

## Growing Impact of ICER Assessments, Particularly in Rare Diseases

ICER assessments inform coverage and formulary decisions at US commercial payers, with research finding 80% of payers consult ICER always or routinely for rare diseases and high-cost therapy areas[1]

## Ultra-Rare Disease Framework Represents an Opportunity to Demonstrate often Unrecognized Value

Since 2017, ICER's modified ultra-rare disease value assessment framework requires presentation of a modified societal perspective co-base case when societal costs are deemed substantial relative to health care costs[2]

## Impact Inventory Defines Potential Societal Impacts for Inclusion

The societal perspective is structured around a defined Impact Inventory spanning sectors including (but not limited to) informal care, productivity, education, and social services[2]

**Abbreviations:** ICER: Institute for Clinical and Economic Review.

# ICER Assessments Using the Ultra-Rare Disease Framework Were Systematically Identified and Analyzed

1. ICER Final Evidence Reports were identified in which the assessed condition met the criteria for the modified ultra-rare disease value assessment framework:[2]
   - Eligible US patient population <10,000 individuals
   - No ongoing or planned clinical trials among the patient population
2. Eligible reports included ≥1 cost-effectiveness analysis from a modified societal perspective
3. Data were extracted on report characteristics, modeled societal impacts (via Impact Inventory tables),* and incremental cost-effectiveness results (utilizing health system and modified societal perspectives)
4. Analyses assessed the prevalence of type of impact included across assessments, the magnitude of change in incremental cost-effectiveness ratios, and the sources used to inform these inputs

*Components included universally under the health system perspective are excluded from this analysis; **Abbreviations:** ICER: Institute for Clinical and Economic Review.

# Six Reports Spanning Neuromuscular, Retinal, and Hematologic Conditions Were Published Between 2018 and 2025

Neuromuscular
Hematologic
Retinal

**July 2018**[3]

*Biallelic RPE65-Mediated Retinal Disease*

Voretigene Neparvovec (Luxturna; **gene therapy**)

**April 2022**[4]

*Duchenne Muscular Dystrophy (DMD)*

Deflazacort (Emflaza; **corticosteriod**)

**July 2022**[5]

*Transfusion–dependent thalassemia (TDT)*

Betibeglogene Autotemcel (beti-cel [Zynteglo]; **gene therapy**)

**August 2023**[6]

*Sickle Cell Disease (SCD)*

Lovo-cel (lovotibeglogene autotemcel; **gene therapy**)

Exa-cel (exagamglogene autotemcel; **gene therapy**)

**May 2025**[7]

*Advanced Retinitis Pigmentosa (RP)**

Sonpiretigene Isteparvovec (MCO-010; **gene therapy**)

**September 2025**[8]

*Spinal Muscular Atrophy (SMA)*

Apitegromab (SRK-015; **monoclonal antibody**)

*This assessment applied both the ultra-rare disease framework and the Single or Short-Term (SST) therapies framework simultaneously, as the condition met both sets of criteria. It is the only instance in our dataset where the societal perspective was included as a scenario rather than a co-base case. **Abbreviations:** ICER: Institute for Clinical and Economic Review; DMD: Duchenne muscular dystrophy; RP: retinitis pigmentosa; SCD: sickle cell disease; SMA: spinal muscular atrophy; TDT: transfusion-dependent thalassemia.

# Included Societal Impacts Varied Substantially Across Assessments

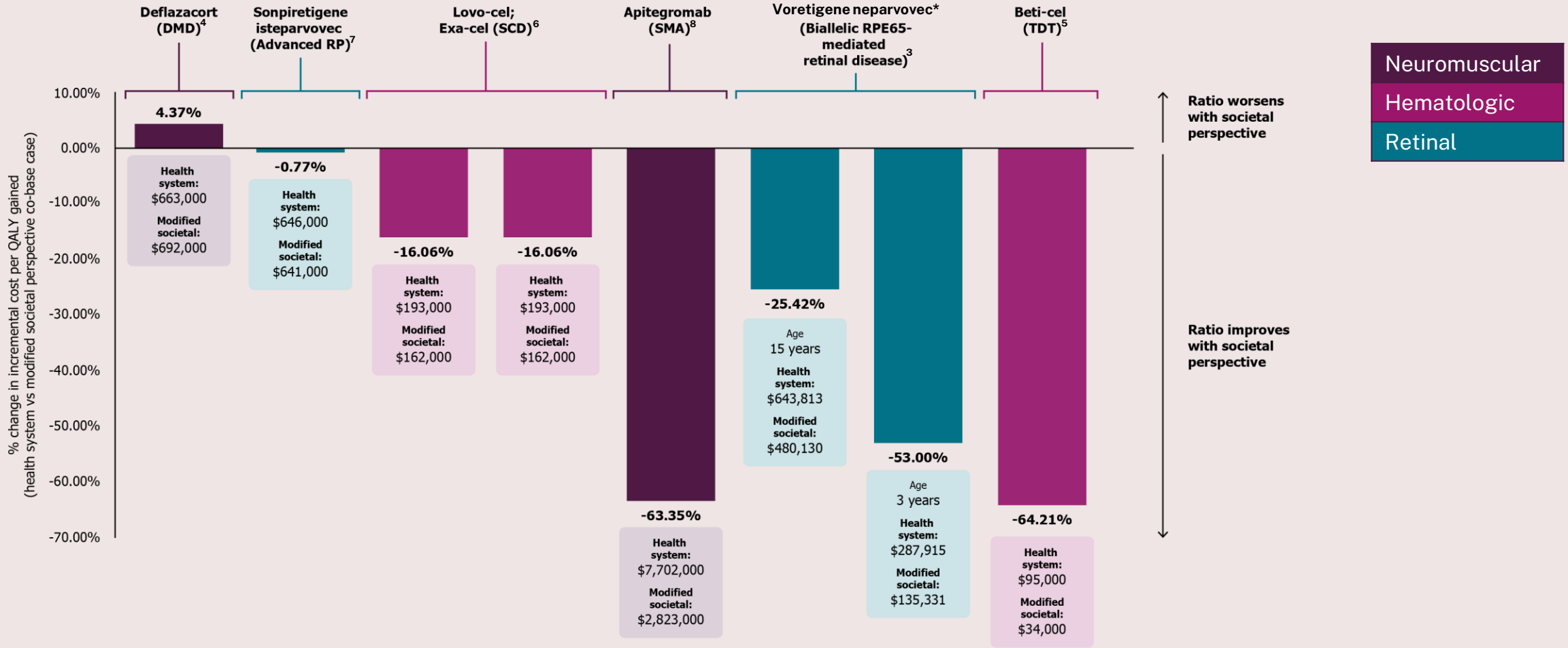
Productivity impacts were most consistently included; impacts related to consumption, legal, housing, and environmental domains appeared in no assessments

| Number of Reports with Impact Included (%) | Type of Impact | Sector* |
|---|---|---|
| 5 (83.3%) | **Labor market earnings lost** | Productivity |
| 5 (83.3%) | **Cost of unpaid lost productivity due to illness** | Productivity |
| 4 (66.7%) | **Unpaid caregiver-time costs** | Health-related costs |
| 4 (66.7%) | **Patient time costs** | Health-related costs |
| 2 (33.3%) | **Caregiver health-related quality of life effects** | Caregiver Health Outcomes |
| 2 (33.3%) | **Cost of uncompensated household production** | Productivity |
| 1 (16.7%) | **Transportation costs** | Health-related costs |
| 1 (16.7%) | **Cost of social services as part of intervention** | Social services |
| 1 (16.7%) | **Impact of intervention on educational achievement of population** | Education |
| 1 (16.7%) | **Medical costs paid by patients out-of-pocket (cost of low vision services and devices)** | Other |

*The following impact sectors were not included in any assessments: consumption, legal/criminal justice, housing, and environmental.

# Across Highly Heterogeneous Assessments, the Societal Perspective Consistently Improved Cost-Effectiveness

In five of six assessments, the modified societal perspective co-base case improved the incremental cost-effectiveness ratio versus the health system perspective alone




*ICER conducted two separate base case analyses for voretigene neparvovec, one reflecting the clinical trial population (mean age 15 years) and one modeling treatment at mean age 3 years. Treatment effect was assumed equal across both cohorts. Differences in results were driven by remaining life expectancy and baseline visual ability at each age.[3] **Abbreviations:** DMD: Duchenne muscular dystrophy; ICER: Institute for Clinical and Economic Review; QALY: quality-adjusted life year; RP: retinitis pigmentosa; SCD: sickle cell disease; SMA: spinal muscular atrophy; TDT: transfusion-dependent thalassemia.

# One Societal Impact Inclusion Decision can Determine Whether the Ratio Improves or Worsens[4]

The co-base case for the DMD assessment excluded caregiver health outcomes. Including them as scenarios shifted the ratio substantially, demonstrating the importance of impact inclusion

| Analysis | Incremental cost | Incremental patient QALYs gained | Incremental caregiver QALYs gained | Total incremental QALYs gained | Incremental cost per QALY gained |
|---|---|---|---|---|---|
| Co-Base Case: Health system perspective | $1,006,000 | 1.52 | - | 8.40 | $663,000 |
| Co-Base Case: Modified societal perspective | $1,050,000 | 1.52 | - | 8.40 | $692,000 |

Deflazacort's extension of ambulation generates additional years of societal costs, including:

- Non-medical community services
- Informal care
- Indirect costs of illness
- Out-of-pocket costs for DMD-related home alterations and uncovered equipment

**Abbreviations:** DMD: Duchenne muscular dystrophy; QALY: quality-adjusted life year.

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| Scenario: Modified societal **+ QALY gains of 1 caregiver** | $1,050,000 | 1.52 | **1.41** | **2.93** | $358,000 |
| Scenario: Modified societal **+ QALY gains of 2 caregivers** | $1,050,000 | 1.52 | **2.82** | **4.34** | $242,000 |

**Abbreviations:** DMD: Duchenne muscular dystrophy; QALY: quality-adjusted life year.

# Only One Prospective, Disease-Specific Source was Used to Model Societal Impacts

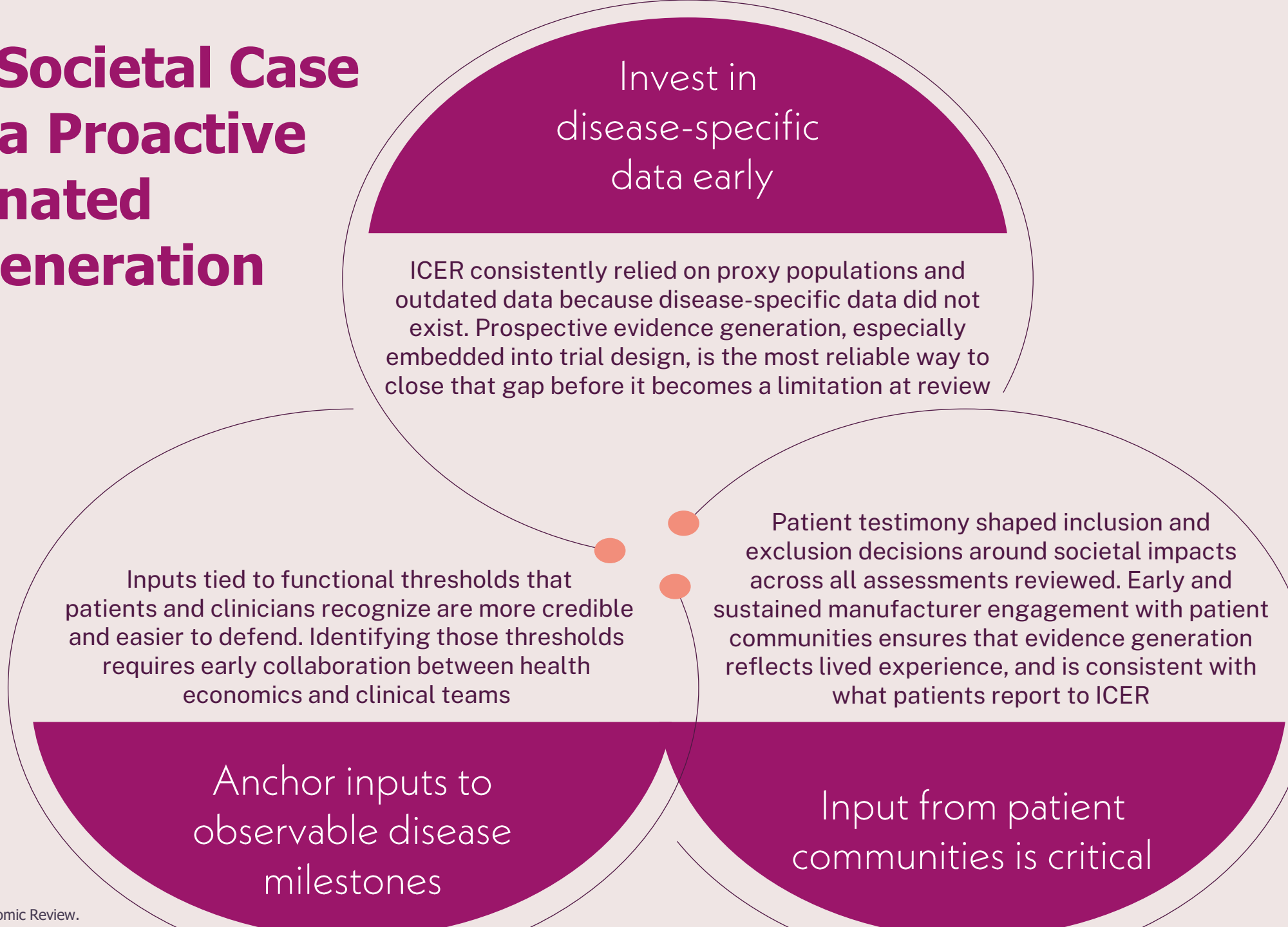
Across the three most commonly included impact sectors, proxy data and cross-sectional sources were the norm, raising questions about the robustness and consistency of societal inputs

Target Population
Proxy Population
Impacts Excluded

| | Productivity | Health-Related Costs | Caregiver Health Outcomes |
|---|---|---|---|
| **RPE65**[3] | Different Disease | Different Disease | Excluded |
| **DMD**[4] | Cross-Sectional | Excluded | Cross-Sectional* |
| **TDT**[5] | **Prospective** | **Prospective** | Different Geography |
| **SCD**[6] | Model Using Survey Data | Cross-Sectional | Excluded |
| **Advanced RP**[7] | Different Disease | Different Disease | Excluded (Patient Input) |
| **SMA**[8] | Excluded (No Available Data) | Excluded | Different Geography |

*DMD caregiver health outcomes were modelled using proxy data as scenario analyses only, and were not incorporated into the co-base case. **Abbreviations:** DMD: Duchenne muscular dystrophy; RP: retinitis pigmentosa; SCD: sickle cell disease; SMA: spinal muscular atrophy; TDT: transfusion-dependent thalassemia.

# A Credible Societal Case Is Built on a Proactive and Coordinated Evidence Generation Strategy




**Abbreviations:** ICER: Institute for Clinical and Economic Review.

# Conclusions

## The societal impacts modeled under the framework were highly variable

- The framework requires a modified societal perspective when societal costs are substantial, but which impacts are included is determined by disease-specific factors and the evidence available to support them
- Patient consultation directly shaped inclusion decisions across all six assessments, in some cases establishing that an impact should be included, in others that it was not applicable to that disease or patient population
- The result is a framework that is consistently structured but highly variable in practice, and that variability is appropriate, provided the decisions are transparent and well-evidenced

## The evidence base is not yet strong enough to support robust models for high-cost ultra rare treatments

- Even the most consistently included impact sectors relied on proxy data, with only one prospective, disease-specific source identified across the entire dataset, and that source was only 23% US-based
- Dimensions of value that could not be quantified were acknowledged but excluded from modeling, including the impact of structural racism and healthcare inequities on SCD outcomes, and mental health impacts across multiple conditions
- This reflects a broader gap in evidence generated for ultra-rare conditions, not a framework limitation

**Abbreviations:** SCD: sickle cell disease.

# Next Steps

## The societal perspective captures value that US payers are not currently structured to act on, but that does not mean it does not matter

- US payers operate within a healthcare cost silo and societal costs fall outside their budget and their mandate
- Only 11% of payers value the inclusion of alternative perspectives such as societal, patient or provider views when reviewing ICER reports, which is structurally expected, not a failure of the framework[1]
- ICER reports are not coverage decisions; they are an input into a broader value conversation

## The case for societal evidence generation is about the future, not just the present

- There is a cycle at work: outputs from societal models are deprioritized partly because the inputs are not robust, and inputs stay weak because the models are deprioritized
- The US system is moving in this direction, with value-based contracting and the IRA creating new pressure to demonstrate comprehensive value beyond healthcare costs alone especially for high-cost therapies with high unmet need
- Disease areas and products with robust societal evidence will be well positioned to enter these discussions

**Abbreviations:** ICER: Institute for Clinical and Economic Review; IRA: Inflation Reduction Act.

# References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For more information about our services, please don't hesitate to get in touch or visit us at booth #440 during the conference.

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